The University of Chicago

THE INFLUENCE OF PITUITARY EXTRACTS ON THE DAILY OUTPUT OF URINE

A DISSERTATION

SUBMITTED TO THE FACULTY
OF THE OGDEN GRADUATE SCHOOL OF SCIENCE
IN CANDIDACY FOR THE DEGREE OF
DOCTOR OF PHILOSOPHY

DEPARTMENT OF PHYSIOLOGY

BY
MAURICE HOLMES REES

Private Edition, Distributed By
THE UNIVERSITY OF CHICAGO LIBRARIES
CHICAGO, ILLINOIS

Reprinted from
THE AMERICAN JOURNAL OF PHYSIOLOGY, Vol. XLV, No. 4
March 1918

The University of Chicago

THE INFLUENCE OF PITUITARY EXTRACTS ON THE DAILY OUTPUT OF URINE

A DISSERTATION

SUBMITTED TO THE FACULTY
OF THE OGDEN GRADUATE SCHOOL OF SCIENCE
IN CANDIDACY FOR THE DEGREE OF
DOCTOR OF PHILOSOPHY

DEPARTMENT OF PHYSIOLOGY

R. UNIV.
BIBLIOTHEEK
LEIDEN

BY
MAURICE HOLMES REES

Private Edition, Distributed By
THE UNIVERSITY OF CHICAGO LIBRARIES
CHICAGO, ILLINOIS

Reprinted from
THE AMERICAN JOURNAL OF PHYSIOLOGY, Vol. XLV, No. 4
March 1918

Digitized by the Internet Archive
in 2026

https://archive.org/details/IA41546811_0055

Reprinted from The American Journal of Physiology, Vol. 45, No. 4,
March, 1918

THE INFLUENCE OF PITUITARY EXTRACTS ON THE DAILY OUTPUT OF URINE

MAURICE H. REES

From the Hull Physiological Laboratory of the University of Chicago

Received for publication January 22, 1918

INTRODUCTORY

Since Magnus and Schäfer (1) first pointed out a possible relation between the hypophysis cerebri and renal function, a large amount of work has been done in an attempt to fix this relationship and, if possible, to point out its nature. The results obtained have been quite conflicting. The earlier investigation seemed to show that extracts of the pituitary gland when injected intravenously have a pronounced diuretic effect. The later work would indicate that such extracts give results which are exactly contrary to those obtained by the earlier investigators, namely, an antidiuretic effect.

In this investigation it was our purpose to find out first, whether the subcutaneous injection of pituitary extract will cause any quantitative variation in the daily output of urine; second, whether such injection will in any way affect the quantity of urine excreted and, if so, to find out if possible the factors involved.

LITERATURE

Magnus and Schäfer (1) working on anesthetized animals, concluded that intravenous injection of extracts of the pituitary gland causes a prolonged expansion of the kidney and a greatly increased rate of renal secretion. The diuresis was in every case of short duration, twenty to thirty minutes, while the kidney dilation continued for a longer time. These authors conclude that the extract acts directly on the renal epithelium in bringing about the increased flow of urine.

This work was later repeated by Schäfer and Herring (2) who arrived at practically the same conclusions. Their results, however, were quite inconstant. In a series of thirteen experiments on dogs, nine show

a diuretic and four an antidiuretic effect after injection. In another series on nineteen rabbits, diuresis was obtained in fourteen cases and a decrease in flow in five cases.

The theory of direct stimulation of the renal cells was also upheld by Hoskins and Means (3), who considered that the direct stimulation may be assisted by a vasodilation in the kidneys.

Houghton and Merrill (4) failed to find any direct action of pituitary extracts on the renal epithelium in the case of perfused kidneys. They conclude that diuresis is caused by an increase in the blood pressure.

Vasodilation of the renal vessels is considered by King and Stoland (5) to be the principal factor involved in the increased flow of urine which they find after pituitary extract injection.

Dale (6) working with perfused kidneys of the dog and cat found that pituitary extracts cause a vasoconstriction of renal vessels. These results were confirmed by Houghton and Merrill (4).

Pal (7) states that isolated rings of the proximal portion of the renal artery are constricted while rings from the peripheral portions of this artery are dilated by pituitrin.

The investigations of Falta, Newburg and Noble (8) indicate that diuresis generally results from subcutaneous injections of pituitary extracts.

A number of other investigators using practically the same methods as those of Schäfer and Herring have reported that diuresis results from the injection of extracts from the pituitary gland.

Within the past three years several investigators have reported that subcutaneous injection of pituitary extracts gives a diuresis of several hours duration. Pentimalli and Quercia (9) found that on the isolated kidney of the rabbit pituitary extract gave a diminished flow from both the ureter and from the renal vein. The decrease was especially marked in the flow from the vein. On the other hand Gabriels (10) reported that in the isolated kidney of the dog pituitary extract caused an increased flow of urine without vasodilation.

A large portion of the evidence in favor of the antidiuretic effect of posterior lobe extract comes from the clinical side where the extract has been used with apparent success in reducing the diuresis of diabetes insipidus. One of the first to report evidence of this nature was Farmi (11) who reported that he had been successful in reducing the diuresis in two diabetes insipidus patients by subcutaneous injections of extract of the pituitary.

Further evidence from the clinical side has been given by von der Velden (12), Konschegg and Schuster (13), Motzfeldt (14), (15) and Bab (16). Most of these investigators have checked up their results experimentally.

Meyenberg (17), working on rabbits and cats, found that subcutaneous injection produced an antidiuresis lasting for eight or ten hours.

Römer (18) found that animals catheterized every hour showed a very marked decreased output of urine after injection with pituitary extract.

The most extensive experimental work showing an antidiuretic effect from the injection of posterior lobe extract has been reported by Motzfeldt (19). Working with a large number of animals, mostly rabbits, he found that subcutaneous injection of the extract gave without exception a marked antidiuresis extending over several hours. Motzfeldt concludes that the results from his experiments on rabbits tend to show that pituitary extracts produce an antidiuretic action on account of their stimulation of the sympathetic nervous system and thus affecting the renal vasomotor system, that is, the direct cause of the antidiuresis is considered as due to vasoconstriction in the kidneys.

METHODS AND RESULTS

In all of our work we have followed rather closely the methods suggested by Motzfeldt with the important exceptions that our observations extended over much longer periods of time and the urinary output was always computed on the twenty-four hour or daily basis.

The experimental observations were made on cats and rabbits. Rabbits were found to be much more susceptible to pituitary extracts than were dogs or cats.

Three commercial extracts were used, namely, Pituitrin (Parke, Davis & Co.), Hypophyseal Solution (Squibb & Co.) and Pituitary Liquid (Armour & Co.). Practically no difference was found in the action of these preparations.

The injections were made subcutaneously in every case. The usual amount injected per day was 1 cc. for cats and 0.5 cc. for rabbits. The injections were made at the beginning of experiment at the time that the water was given by stomach tube.

Ordinary aseptic precautions were used in making the injections. No infections resulted from the repeated injections.

In order to obtain accurate data on the water intake the water was always given by stomach tube.

The animals were kept in perfectly dry cages and the nature and amount of food given were accurately noted in each case.

The urine was collected in such a way as to avoid so far as possible any evaporation or any contamination with feces.

The daily quantity and the specific gravity were the principal points noted in each experiment. Variations in the rate of output were also noted in the case of the catheterized rabbits.

Tests were made in each experiment for sugar and albumin but these were not observed. In both cats and rabbits the daily output of urine varies widely even with a constant food and water supply. On this account it was found advisable to extend the observations over several days.

In our first series of observations it was our purpose to find out whether pituitary extracts will, when injected subcutaneously, cause any variation in the daily output of urine. In table 1 we give the averages from this series of experiments. By inspection of this table it will be found that the averages for the control animals and for the injected animals are practically the same both in amount and in specific gravity. In six cases there is a slight decrease in the daily output of the injected animals but this is balanced by four cases where there is a greater increase in daily output. The variations above and below the mean were, with the exception of one case, less than 11 cc.

There is no indication that the animals established a resistance to pituitary extract after repeated injections. In practically every case the daily output of urine following the first and second injections was as high as that obtained on the ninth or tenth days of injections.

Attempts were made to study the effect of doses larger than 1 cc. per day, but these did not yield satisfactory results on account of the systemic disturbances caused. In the case of cats, vomiting was the most common result from large doses, in fact, even with 1 cc. doses a number of cats had to be rejected on account of this tendency to vomit following the injections. The vomiting may not occur until thirty or forty minutes after the water and the injections have been given. For this reason it is necessary to watch the animals closely for at least this length of time, so that one may be sure that he is not including regurgitated water in the urine measurements.

The apparent decrease in daily output of urine after injection shown in table 2 may be accounted for by the loss of water due to the increased defecation.

TABLE 1

Summary of experiments on the influence of pituitary extract on the urinary output in cats. The averages for each animal are computed from ten days of normal (control) and from ten days of daily injection with 1 cc. of pituitary extract. Each animal was given 100 grams of cooked meat per day. Water was given by stomach tube

		AMOUNT OF WATER GIVEN PER DAY	URINE	
			Average amount per day	Average specific gravity
		cc.	cc.	
A. Female; weight 2600 grams	Control	100	103.9	1014.5
	Pituitary extract	100	114.2	1011.3
B. Female; weight 2750 grams	Control	100	104.1	1013.8
	Pituitary extract	100	107.1	1013.3
C. Male; weight 2900 grams	Control	100	101.8	1025.6
	Pituitary extract	100	103.0	1024.8
D. Female; weight 2750 grams	Control	50	68.0	1021.2
	Pituitary extract	50	62.3	1019.8
E. Female; weight 2700 grams	Control	50	64.1	1027.4
	Pituitary extract	50	57.1	1030.0
F. Male; weight 2800 grams	Control	200	175.2	1008.6
	Pituitary extract	200	165.4	1010.4
G. Male; weight 2860 grams	Control	100	95.0	1015.4
	Pituitary extract	100	117.6	1016.0
H. Female; weight 2680 grams	Control	20	41.6	1044.0
	Pituitary extract	20	33.6	1040.0
I. Female; weight 2710 grams	Control	20	46.8	1044.0
	Pituitary extract	20	40.8	1045.0
J. Male; weight 2890 grams	Control	20	30.6	1043.0
	Pituitary extract	20	26.1	1045.0

In attempting to inject doses larger than 2 cc. per day no satisfactory results were obtained. In two cases the output was reduced to one-half the normal. In three cases there was a very marked increase in daily output. The usual result, however, was that it was impossible to keep the injected animals from regurgitating the water introduced by stomach tube.

Rabbits gave practically the same results as cats so far as the effect of pituitary extracts upon daily output and specific gravity of the urine is concerned. This is shown in tables 3, 4 and 5.

The variation between the control and the injected animals was greater in the experiments on rabbits than in those on cats. This is accounted for in part by the shorter time covered by the rabbit experiments. It was not possible to keep the rabbits in good condition for

TABLE 2

Effect of large doses of pituitary extracts on urinary output in cat. Pituitary extract was given in two doses per day of 1 cc. each at six hour interval. Animal was given daily 100 grams of cooked meat and 150 cc. of water by stomach tube

	DAY	URINE	
		Cubic centimeters	Specific gravity
Control	1	183	1010
	2	163	1010
	3	155	1010
Injected	4	108	1009
	5	173	1014
	6	165	1014

longer periods of experimentation than those used. In order to avoid the loss of excessive amounts of water in the large amount of feces passed, it was found advisable to reduce the food supply to such an extent that a very small amount of material was normally passed from the intestine. The reduced food supply was also found to be necessary to avoid the development of diarrhea following the injections.

Another cause for the variation in the case of rabbits may be found in the tendency of the pituitary extract to increase defecation. This fact is referred to later in another connection.

The second part of our problem was to find out whether the subcutaneous injection of pituitary extract causes any variation in the rate of urinary excretion. Rabbits were found to be best suited for this line of work since by using males it was easy to collect the urine at regular

intervals by catheterization. Silk linen catheters no. 11 were found to be best adapted for this purpose.

It was found necessary to select rabbits that could be catheterized with ease since irritation of the urethra apparently exerted a reflex inhibition on the kidney. Rabbit 3 in table 4 illustrates this point.

Tables 4 and 5 show the effect of pituitary extracts on the rate of

TABLE 3

Summary of experiments on the influence of pituitary extracts on daily urinary output in rabbits. The averages for each animal are computed from three days of normal (control) and three days with daily injection of 0.5 cc. of pituitary extract. Each animal was given 50 grams of cabbage per day, 150 cc. of water was given daily to each animal

		URINE	
		Average amount per day	Average specific gravity
		cc.	
5. Male; weight 1677 grams	Control	139.6	1012.6
	Pituitary extract	181.3	1018.0
6. Male; weight 1774 grams	Control	139.3	1013.3
	Pituitary extract	181.6	1014.0
7. Male; weight 1810 grams	Control	201.6	1016.6
	Pituitary extract	191.3	1011.6
8. Male; weight 1751 grams	Control	192.3	1007.3
	Pituitary extract	212.0	1013.6
9. Male; weight 1698 grams	Control	180.0	1010.0
	Pituitary extract	257.0	1012.3
10. Male; weight 1830 grams	Control	227.6	1010.0
	Pituitary extract	187.6	1012.0

secretion, but this is even better shown in figure 1. It will be noted from the figure that the normal diuresis which follows the giving of 150 cc. of water to rabbits by stomach tube reaches its maximum in the second or third hour after giving the water. By the end of the seventh hour the diuresis has practically exhausted itself and the normal excretion of 2 to 3 cc. per hour follows. After the injection of pituitary extract the picture is quite different.

In this case the diuresis is held in check for seven or eight hours when it breaks through and may reach a level as high as that of normal secretion. As a rule the diuresis following the injection is prolonged for ten to twelve hours. The total output per day is found to be practically the same in both cases.

By referring to some of Motzfeldt's (15) figures it will be noted that they show an increase in urine output in the seventh and eighth hours,

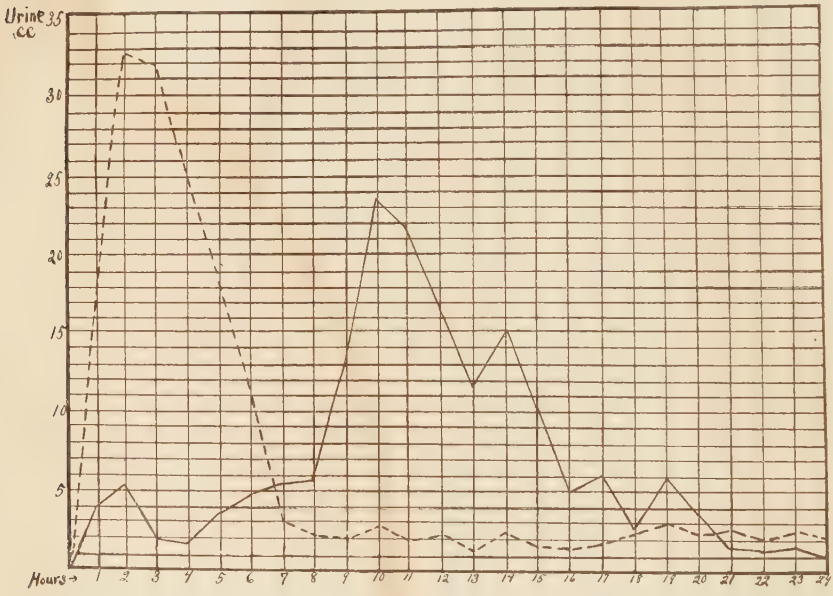

Fig. 1. Curves showing the effect of pituitary extract on urinary output. Each curve is plotted from averages from two animals (rabbits). At the beginning of the experiment each animal was given 150 cc. of water per os. The injected animals were each given 0.5 cc. of pituitary extract subcutaneously at the beginning of the experiment. The broken line represents the control animals. The continuous line represents the injected animals. Average 24 hours urinary output of control animals, 172.6 cc. Average 24 hours urinary output of injected animals, 170.5 cc.

that is, his observations were carried just to the beginning of the diuresis which has been delayed by the pituitary extract.

The third problem which concerned us was the cause of the delay in diuresis which we found followed the subcutaneous injections of pituitary extract. Several things which appeared in the course of the

experiments suggested to us that delayed absorption from the alimentary canal may be an important factor in causing this delayed diuresis. It has already been noted that in the case of injected cats there is a pronounced tendency to vomit. The vomiting may occur three-quarters of an hour after giving the water and the injection. Usually four- to five-sixths of the water was returned in the vomit, indicating that there

TABLE 4

Effect of pituitary extract on the urinary output in rabbits. Each animal was given 150 cc. of water by stomach tube at the beginning of the experiment. No food was given during the experiment. Rabbits 1, 2 and 3 were injected at the beginning of the experiment with 1 cc. of pituitary extract. The urine was drawn by catheterization

	(1) Male; weight 1720 grams pituitary extract urine	(2) Male; weight 1780 grams pituitary extract urine	(3) Male; weight 1675 grams pituitary extract urine	(4) Male; weight 1930 grams control urine
	cc.	cc	cc.	cc
6.00 a.m.				
6.30 a.m.	5.0	3.0	2.5	2.5
7.00 a.m.	20.0	4.0	4.0	5.0
7.30 a.m.	15.0	2.0	2.0	13.0
8.00 a.m.	4.0	1.5	2.0	13.0
8.30 a.m.	4.5	3.5	1.5	19.0
9.00 a.m.	0.5	5.0	1.0	18.0
9.30 a.m.	4.0	10.0	1.0	16.0
10.00 a.m.	9.0	5.0	1.5	0.5
10.30 a.m.	4.0	4.0	1.5	24.0
11.00 a.m.	0.5	2.0	2.0	7 0
11.30 a.m.	1.0	2.0	0.5	0.0
12.00 m.	3.5	2.5	1.5	5.5
Total first 6 hours.....	71.0	46.0	20.0	123.5
6.00 p.m.	56.5	57.5	11.5	18 5
6.00 a.m.	91.0	48.0	51.0	31.0
Total 24 hours.....	218.5	151.5	82.5	173.0

was a delay in passing the water from the stomach. The injection of large doses of the extract commonly caused diarrhea. The effect of the extract on the alimentary canal was much more pronounced in rabbits than in cats. Rabbits kept on a uniform diet of 50 grams per day of carrots or cabbage pass very small amounts of feces in the form of comparatively dry pellets. After injection with 0.5 cc. of pituitary extract there is a marked increase in the amount of feces which are of a

TABLE 5

Periodic variation in output of urine in male rabbits following injection of pituitary extracts. Each animal was given daily 50 grams of carrots and 150 cc. of water by stomach tube. The water and the pituitary extract were given at the beginning (6 a.m.) of the experiment. Injected animals received 0.5 cc. of pituitary extract subcutaneously

		DATE	TIME	URINE		Total amount urine per day
				Cubic centimeters	Specific gravity	
				cc		
11. Weight 1934 grams	Control	May 29–30	12 m.	101.0	1010	
			6 p.m.	0.0		
	Pituitary extract		6 a.m.	103.0	1006	204.0
		May 30–31	12.00 m.	34.0		
			6.00 p.m.	15.0		
			6.00 a.m.	95.0	1010	154.0
12. Weight 1677 grams	Control	May 29–30	12.00 m.	122.0	1005	
			6.00 p.m.	16.0		
	Pituitary extract		6.00 a.m.	30.0		154.0
		May 30–31	12.00 m.	18.5		
			6.00 p.m.	29.0		
			6.00 a.m.	134.0	1009	181.5
13. Weight 1740 grams	Control	May 29–30	12.00 m.	108.0		
			6.00 p.m.	17.0		
	Pituitary extract		6.00 a.m.	42.0		167.7
		May 30–31	12.00 m.	40.0	1004	
			6.00 p.m.	0.0		
			6.00 a.m.	45.0	1015	85.0
14. Weight 1734 grams	Control	May 29–30	12.00 m.	133.0	1004	
			6.00 p.m.	12.0		
	Pituitary extract		6.00 a.m.	38.0		183.0
		May 30–31	12.00 m.	37.0		
			6.00 p.m.	88.0	1002	
			6.00 a.m.	95.0	1010	220.0
15. Weight 2085 grams	Control	May 29–30	12.00 m.	158.0	1005	
			6.00 p.m.	17.0		
	Pituitary extract		6.00 a.m.	11.0		186.0
		May 30–31	12.00 m.	23.0		
			6.00 p.m.	30.0		
			6.00 a.m.	133.0	1007	186.0

TABLE 5—*Continued*

		DATE	TIME	URINE		Total amount urine per day
				Cubic centimeters	Specific gravity	
						cc.
16. Weight 2027 grams	Control	May 29–30	12.00 m.	145.0	1006	
			6.00 p.m.	27.0		
			6.00 a.m.	16.0		188.0
	Pituitary extract	May 30–31	12.00 m.	35.0		
			6.00 p.m.	43.0	1015	
			6.00 a.m.	87.0	1015	165.0
17. Weight 2285 grams	Control	May 29–30	12.00 m.	145.0	1008	
			6.00 p.m.	25.0		
			6.00 a.m.	5.0		175.0
	Pituitary extract	May 30–31	12.00 m.	43.0		
			6.00 p.m.	11.0		
			6.00 a.m.	133.0	1012	187.0
18. Weight 2640 grams	Control	May 29–30	12.00 m.	135.0	1008	
			6.00 p.m.	63.0		
			6.00 a.m.	35.0		234.0
	Pituitary extract	May 30–31	12.00 m.	42.0	1024	
			6.00 p.m.	2.0		
			6.00 a.m.	123.0	1012	167.0

semifluid consistency. This excessive amount of water feces accounts for the apparent decrease in the daily urinary output found in some cases after injection. An example of this is seen in rabbits 13 and 18 in table 5.

If rabbits are injected with doses of 1 cc. or more, large masses of semi-fluid feces are thrown off in five to ten minutes after giving the water and the injection. The large amount of water given was not the direct cause of the diarrhea since the controls passed small amounts of feces in the usual pellet form.

The effect of pituitary extracts on absorption was tested experimentally. The results indicate that there is a retarding of absorption after subcutaneous injection of the extract.

In order to avoid the possible effect of the anesthetic on the rate of absorption, a decerebrated dog was used in the following experiment.

When a diuresis was produced by the constant intravenous injection with the Woodyatt injection apparatus of 150 cc. of 0.9 sodium chloride

TABLE 6

Effect of pituitary extract on intestinal absorption in the cat. The animal was anesthetized lightly by giving urethane (2 grams per kilo) per os. The small intestine was exposed and washed, then ligated at either end

	AMOUNT OF WATER INJECTED INTO SMALL INTESTINE	WATER RECOVERED AFTER 1 HOUR	ABSORPTION
	cc.	cc.	cc.
Control animal	30	8	22
Injected animal 1 cc. pituitary extract, subcutaneously	30	27	3

solution per kilo per hour, the subcutaneous injection of pituitary extract had no effect on it (three experiments). On the other hand the injection of the extract caused a delay in the diuresis caused by giving 150 cc. of 0.9 salt solution by stomach tube.

The fact that the rate of diuresis caused by giving 0.9 NaCl solution intravenously is not affected by subcutaneous injection of pituitary extracts but is affected by such injections when the salt solution is introduced into the alimentary canal would indicate that the extract in some way causes delayed intestinal absorption.

TABLE 7

Effect of pituitary extract on intestinal absorption in the rabbit. Anesthetized and intestine prepared as in table 6

	AMOUNT OF WATER INJECTED INTO SMALL INTESTINE	WATER RECOVERED AFTER	ABSORPTION
	cc.	cc	cc.
Control animal	30	0	30
Injected animal 0.5 cc. pituitary extract subcutaneously	30	25	5

TABLE 8

Effect of pituitary extracts on intestinal absorption in a decerebrated dog. A 14 inch loop from the middle of the jejunum was used

	AMOUNT OF WATER INJECTED INTO INTESTINE	WATER RECOVERED AFTER 30 MINUTES	ABSORPTION
	cc.	cc.	cc.
Control period	75	42	32
Injected period	75	70	5

The fact that pituitary extract does not affect the diuresis following intravenous injection of normal salt solution would also indicate that the extract does not regulate the diuresis by an action on the salt content of the blood as has been recently advocated by Abrahamson and Climenko (20).

TABLE 9

Effect on the diuresis produced by giving 150 cc. of 0.9 NaCl solution per os in rabbits

		DATE	TIME	URINE		TOTAL AMOUNT URINE PER DAY
				Cubic centimeters	Specific gravity	
						cc.
	Controls	July 25–26	12.00 m.	86	1013	
			6.00 p.m.	28		
			6.00 a.m.	42		156
Rabbit 19; male; weight 2100 grams	Controls	July 26–27	12.00 m.	122	1011	
			6.00 p.m.	51		
			6.00 a.m.	47	1019	220
	Pituitary extract 0.5 cc. per day	July 27–28	12.00 m.	82	1018	
			6.00 p.m.	94		
			6.00 a.m.	90		266
		July 28–29	12.00 m.	58		
			6.00 p.m.	55		
			6.00 a.m.	77	1013	190
	Controls	July 25–26	12.00 m.	182	1010	
			6.00 p.m.	58		
			6.00 a.m.	52	1024	292
Rabbit 20; male; weight 1550 grams	Controls	July 26–27	12.00 m.	114	1015	
			6.00 p.m.	70		
			6.00 a.m.	61	1025	245
	Pituitary extract 0.5 cc. per day	July 27–28	12.00 m.	97	1012	
			6.00 p.m.	63		
			6.00 a.m.	122	1022	282
		July 28–29	12.00 m.	90		
			6.00 p.m.	47		
			6.00 a.m.	73	1025	210

Previous workers have shown that subcutaneous injection of pituitary extracts does not affect the general blood pressure in anesthetized animals. We found that in decerebrated animals subcutaneous injection of the extract had no effect on blood pressure (two experiments). The effect of the extract on the rate of urinary excretion can not then be due to any general vasomotor change. It is possible, however, that

there may be a vasoconstriction in minute vessels of the intestinal wall thus causing a delayed absorption and incidentally a delay in the diuresis. This does not necessarily rule out the possibility that there may also be a simultaneous vasoconstriction in the kidney which is also a factor in retarding the diuresis.

CONCLUSIONS

1. Subcutaneous injections of pituitary extract do not alter quantitatively the daily output of urine in cats and rabbits, nor do they cause any marked variation in the specific gravity of the urine.

2. The subcutaneous injection of pituitary extracts causes a delay of seven to eight hours before the beginning of the diuresis which follows the ingestion of large amounts of water. This delay, however, does not cause any variation in the total amount of urine excreted in twenty-four hours.

3. The delay in diuresis which is produced by subcutaneous injection of pituitary extract is due in part at least to a delayed absorption from the alimentary canal.

4. The subcutaneous injection of pituitary extract has no influence on the diuresis induced by a continuous intravenous injection of isotonic salt solution.

BIBLIOGRAPHY

(1) Magnus and Schäfer: Journ. Physiol., 1901, xxvii, 9.
(2) Schäfer and Herring: Phil. Trans. Roy. Soc. London, 1908, cxcix, 1.
(3) Hoskins and Means: Journ. Pharm. Exper. Therap., 1912, iv, 435.
(4) Houghton and Merrill: Journ. Amer. Med. Assoc., 1908, li, 1849.
(5) King and Stoland: This Journal, 1913, xxxii, 405.
(6) Dale: Biochem. Journ., 1909, iv, 427.
(7) Pal: Wiener med. Wochenschr., 1909, lix, 137.
(8) Falta, Newberg and Noble: Zelin. Med., 1911, lxxii, 97.
(9) Pentimalli and Quercia: Arch. Ital. Biol., 1912, lviii, 33.
(10) Gabriels: Arch. Internat. Physiol., 1913, xiv, 428.
(11) Farmi: Wiener klin. Wochenschr., 1913, 1867.
(12) Von der Velden: Berl. klin. Wochenschr., 1913, v, 2083.
(13) von Konschegg and Schuster: Deutsch. med. Wochenschr., 1915, xli, 1091.
(14) Motzfeldt: Norsk. Mag. Loegevidensk., 1914, lxxv, 1292.
(15) Motzfeldt: Boston Med. Surg. Journ., 1916, clxxiv, 644.
(16) Bab: Münch. med. Wochenschr., 1916, lxxiii, 1758.
(17) von Meyenburg: Beitr. Path. Anat., 1916, lxi, 550.
(18) Römer: Deutsch. med. Wochenschr., 1914, xl, 108.
(19) Motzfeldt: Journ. Exper. Med., 1917, xxv, 153.
(20) Abrahamson and Climenko: Journ. Amer. Med. Assoc., 1917, lxix, 281.